WHAT IS CLAIMED:

What is claimed is:

1. A coronavirus inhibitor which is selected from the group consisting of

a) a Five-Helix protein,

b) an HR2 peptide,

c) an HR1 peptide,

d) an HR1 chimeric peptide,

e) a D-peptide which is the retro-inverso analogue of b), c), or d); and

f) a modified version of b), c), or d), containing one or more modifications selected from the group consisting of i) one or more tryptophan analogs, ii) one or more lactam bridges, and iii) one or more protecting groups.

2. The inhibitor of claim 1 which is derived from S protein of human SARS-CoV.

3. The inhibitor of claim 2 further comprising a capping residue on the N-terminus, the C-terminus or both.

4. The inhibitor of claim 3 wherein the capping residue on the N-terminus is selected from the group consisting of T, D and S and the capping residue on the C-terminus is selected from the group consisting of G, R, H, N, and K.

5. The inhibitor of claim 2 further comprising an amino-terminal cap.

6. The inhibitor of claim 5 wherein the amino-terminal cap is acetyl or succinimide.

7. A method of identifying a drug candidate that inhibits coronavirus infection, comprising combining a compound and the inhibitor of claim 1, under conditions appropriate for binding of the compound and the inhibitor to occur, and determining if binding occurs.

8. The method of claim 7 further comprising determining if the compound that binds the inhibitor inhibits coronavirus infection of mammalian cells in a cell-based assay.

9. A method of inhibiting coronavirus infection of cells in an individual, comprising administering to the individual the inhibitor of claim 1 in sufficient quantity and by an appropriate route, whereby infection of cells in the individual is inhibited.

10. The inhibitor of claim 1 which is a Five-Helix protein being soluble under physiological conditions and comprising three heptad repeat 1 components of coronavirus S2 protein and at least two,

but not three complete, heptad repeat 2 components of coronavirus S2 protein, wherein the components are separated by linkers.

11. The inhibitor of claim 1 wherein the Five-Helix protein has an amino acid sequence selected from the group consisting of:

the sequence of residues 1-243 of SEQ ID NO:34,
the sequence of residues 1-237 of SEQ ID NO:35,
the sequence of residues 1-237 of SEQ ID NO:36, and
the sequence of residues 1-317 of SEQ ID NO:37.

12. The inhibitor of claim 1 which is an HR2 peptide comprising at least 20 amino acid residues from coronavirus HR2 and is an inhibitor of coronavirus infection of eukaryotic cells.

13. The inhibitor of claim 12 wherein the HR2 peptide has a sequence selected from the group consisting of: amino acid residues 5-50, 9-41, 21-57, 5-41, 30-57, and 1-57 of SEQ ID NO:2, and 1148-1182 and 1148-1185 of SEQ ID NO:1.

14. The inhibitor of claim 1 which is an HR1 chimeric peptide having an amino acid sequence selected from the group consisting of:

a peptide consisting of SEQ ID NO:16, or residues 2-63 of SEQ ID NO:16;
a peptide consisting of SEQ ID NO:17, or residues 2-67 of SEQ ID NO:17;
a peptide consisting of SEQ ID NO:18;
a peptide consisting of SEQ ID NO:19;
a peptide consisting of SEQ ID NO:20;
a peptide consisting of SEQ ID NO:21, or residues 2-56 of SEQ ID NO:20;
a peptide consisting of SEQ ID NO:22, or residues 2-49 of SEQ ID NO:21;
a peptide consisting of SEQ ID NO:23, or residues 2-53 of SEQ ID NO:22;
a peptide consisting of SEQ ID NO:24, or residues 2-67 of SEQ ID NO:23;
a peptide consisting of SEQ ID NO:25, or residues 2-63 of SEQ ID NO:24;
a peptide consisting of SEQ ID NO:26;
a peptide consisting of SEQ ID NO:27;
a peptide consisting of SEQ ID NO:28, or residues 1-49 of SEQ ID NO:25;
a peptide consisting of SEQ ID NO:29, or residues 1-49 of SEQ ID NO:26;
a peptide consisting of SEQ ID NO:30;
a peptide consisting of SEQ ID NO:31; and
a peptide consisting of SEQ ID NO:32.

15. The inhibitor of claim 1 which is an HR1 peptide comprising about 28 amino acid residues from HR1 of a coronavirus.

16. The inhibitor of claim 15 wherein the HR1 peptide have an amino acid sequence comprising amino acid residues from about amino acid residue 900 to amino acid residue 974 of the sequence of SEQ ID NO:1 or amino acid residues from about 889 to about 1005 of the sequence of SEQ ID NO:1.

17. The inhibitor of claim 16 wherein the amino acid sequence is selected from the group consisting of sequences of residues 896-972, 900-938, 914-949, 922-956, 943-980, and 943-981 of SEQ ID NO:1.

18. The inhibitor of claim 1 which is the retro-inverso analogue of an HR2 peptide, an HR1 peptide, or an HR1 chimeric peptide.

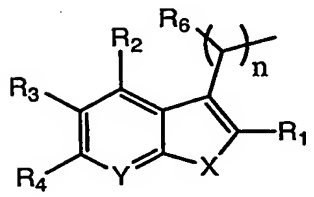
19. The inhibitor of claim 1 comprising,

an HR region selected from the HR1 or HR2 sequence of coronavirus, optionally modified with one or more conservative substitutions, and

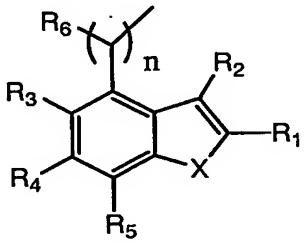
one or more tryptophan analogs,

wherein said one or more tryptophan analogs may be present in said HR based region or an additional amino acid region located at the N-terminus or C-terminus of said HR based region.

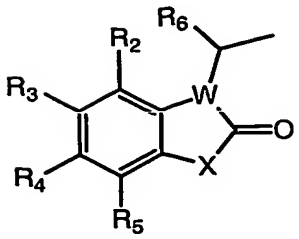
20. The peptide of claim 19, wherein each tryptophan analog is a modified amino acid having an R group independently selected from the group consisting of:



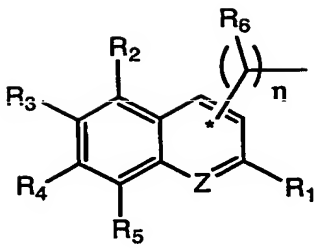
I



II



III



IV

wherein X is O, S, or NR_7;

Y is C-R_5 or N;

W is N or CH;

Z is CH or N;

R_1, R_2, and R_5 are independently selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 alkylamino, amino, and carboxyl;

R_3 and R_4 are either (1) independently selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 alkylamino, amino, and carboxyl; or (2) joined together to provide a fused benzene ring;

R_6 is H or methyl;

R_7 is H or linear, branched or cyclic C_1-C_6 alkyl; and

n is 0 or 1;

further provided that in the case of formula I, R_1 may also be CH_2 where there is a bond from this CH_2 to the alpha-NH of said modified amino acid.

21. The peptide of claim 20, wherein said peptide consists of:

said HR region,

an optionally present N-terminus enhancer group joined to the N-terminus of said HR region, and

an optionally present C-terminus enhancer group joined to the C-terminus of said HR region,

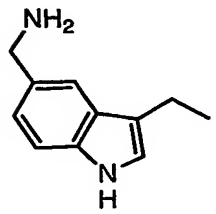
provided that at least one tryptophan analog is present,

further provided that said N-terminus, said C-terminus, or both said N-terminus and C-terminus of said peptide may contain a protecting group.

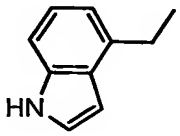
22. The peptide of claim 21, wherein said N-terminus enhancer group is XQEXEQK (SEQ ID NO:38), wherein each X independently is either tryptophan or tryptophan analog.

23. The peptide of claim 21, wherein said C-terminus enhancer group is XPXYVXL (SEQ ID NO:39), or residues 1, 1-2, 1-3, 1-4, 1-5, or 1-6 of SEQ ID NO:39, wherein each X independently is either tryptophan or tryptophan analog.

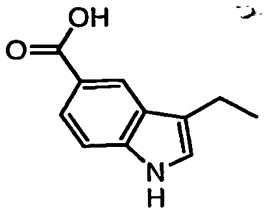
24. The peptides of claims 22-23, wherein each X R group is independently selected from the group consisting of:



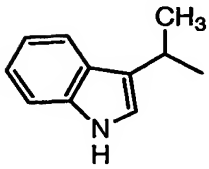
Trp(5-CH_2NH_2)



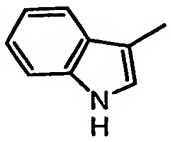
neo-Trp



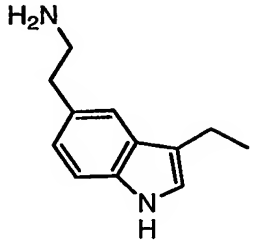
Trp(5-CO_2H)



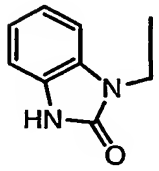
Beta-MeTrp



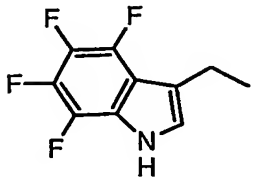
nor-Trp



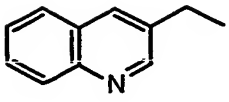
Trp(5-$CH_2CH_2NH_2$)



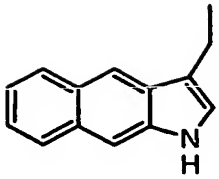
(1-Benzimidazolonyl)alanine



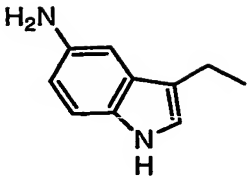
Trp(4,5,6,7-tetrafluoro)



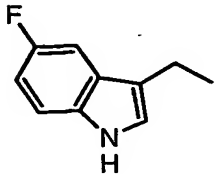
Ala((3-(3-Quinolinyl))



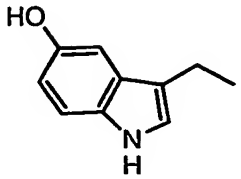
Benzo-Trp



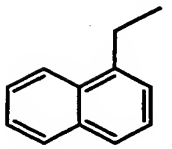
Trp(5-NH_2)



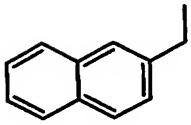
Trp(5-F)



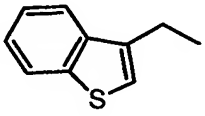
Trp(5-OH)



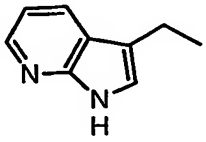
1-naphthylalanine



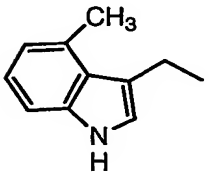
2-naphthylalanine



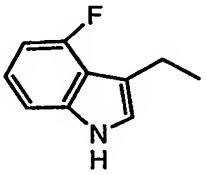
beta-(3-Benzothienyl)Ala



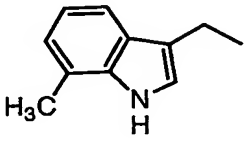
7-azaTrp



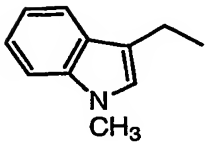
4-MeTrp



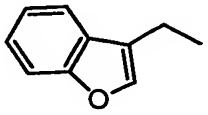
4-F-Trp



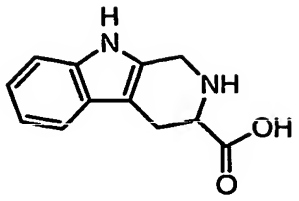
7-MeTrp



1-MeTrp



beta-(3-Benzofuranyl)Ala ; or said modified amino acid is



1,2,3,4-tetrahydro-9H-pyrido(3,4-b)indole-3-carboxylic acid.

25. The inhibitor of claim 1 wherein the inhibitor has an HR region selected from the HR1 or HR2 sequence of coronavirus, optionally modified with one or more conservative substitutions, and is: (a) modified to contain one or more lactam bridges each of which is independently in an (i, i + 3), (i, i + 4) or (i, i +7) orientation; and (b) optionally modified to contain one or more conservative substitutions.

26. The peptide of claim 25 wherein N-terminus, C-terminus, or both the N-terminus and C-terminus of the peptide contain a protecting group.

27. The peptide of claim 25, wherein each of said lactam bridges is independently formed between: (a) an amino acid providing a carboxyl moiety, selected from the group consisting of aspartic acid, glutamic acid, 2-aminohexanedioic acid and 2-aminoheptanedioic acid; and (b) an amino acid providing an amino moiety, selected from the group consisting of lysine, ornithine, diaminobutyric acid, and diaminopropanoic acid.